

REMARKS

This document is filed in reply to the final office action dated December 23, 2003 (“Office Action”). Claims 33-63 are pending. Reconsideration of this application is respectfully requested in view of the following remarks.

The Examiner maintained the rejections against all pending claims under 35 U.S.C. § 103(a) as being obvious on two grounds. Applicant traverses each ground below:

**I**

The Examiner maintained the rejection against claims 33-36, 41-46, 51-53, and 58-59 over Zhang et al., J. Biol. Chem. 270(15): 8501-8505 (“Zhang”) in view of Miller et al., Biotechniques 7(9): 980-990, 1989 (“Miller”). See the Office Action, page 2, lines 14-17. Applicant disagrees and discusses independent claim 33 first.

Claim 33 covers a viral expression vector containing (1) a transcriptional start site, (2) a promoter operably linked to the transcriptional start site, and (3) an enhancer operably linked to the promoter. The enhancer contains a nucleotide sequence of SEQ ID NO: 1 or its complement.

Zhang teaches a non-viral expression vector having a  $\zeta$ -globin promoter operably linked to an HS40 enhancer and a transcription start site. The HS40 enhancer contains the sequence of SEQ ID NO: 1. Miller teaches retroviral vectors N2 and LNL6, each of which contains a promoter operably linked to a gene of interest and a polyadenylation signal. Neither reference teaches or suggests a viral vector containing an enhancer, such as that resulted in claim 33.

Nonetheless, according to the Examiner, it would have been obvious to one skilled in the art to include in the Miller vectors the vector elements taught in Zhang, including the HS40 enhancer. In the response filed on July 24, 2003, Applicant pointed out that it is well known in the art that an enhancer that functions in a non-viral vector, such as the Zhang vector, may not function in a viral vector. As a result, one skilled in the art would not have been motivated to make a viral vector containing an enhancer in the way suggested by the Examiner. To support this point, Applicant submitted a copy of McCune et al. (“McCune”), which teaches that (1) an enhancer functions well in a non-viral vector, but fails in a viral vector and (2) viral vector sequences are responsible for the failure.

However, the Examiner countered that “[the] element as taught by McCune is not limited to the response element as claimed, i.e., SEQ ID NO: 1.” See the Office Action, page 3, lines 28-29. It appears to be the Examiner’s position that McCune should not be considered as it does not recite the sequence of SEQ ID NO: 1. Here, we note that “[t]he test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art, and all teachings in the prior art must be considered to the extent that they are in analogous arts.” (Emphasis added). See MPEP 2143.01. McCune relates to “general problem of sustaining expression of retrovirus-transduced genes in primary tissues (see page 4477, column 2, lines 12-13).” Zhang discusses DNA motifs regulating human  $\alpha$ -like globin gene expression (page 8501, the abstract, lines 1-2).” Miller relates to “Improved Retroviral Vectors for Gene Transfer and Expression (see the title).” Clearly, all three references “are in analogous arts” and therefore “must be considered.” It is improper to consider only Zhang and Miller, and disregard McCune.

The Examiner further asserted that “applicant fails to consider the combined teachings of [Zhang and Miller] in entirety … [applicant’s] arguments … rely heavily on the [individual] deficiencies of each reference….” Applicant disagrees. In fact, contrary to the Examiner’s assertion, Applicant did not rely on individual deficiencies of each reference. Instead, Applicant pointed out deficiencies common to both references. That is, the two references, alone or combined, (1) did not teach a viral vector containing an enhancer, and (2) would not have motivated one skilled in the art to make such a viral vector. Indeed, since McCune teaches that an enhancer does not function at all in a viral vector, in view of all three references, one skilled in the art would be taught away from an enhancer-containing viral vector, such as that of claim 33.

Thus, claim 33 is clearly not rendered obvious by Zhang and Miller. Claim 51 covers a method using the expression vector of claim 33 and is therefore also not rendered obvious by these two references for the same reasons. Neither are claims 34-36, 41-46, 52-53 and 58-59, all of which depend from claims 33 and 51 directly or indirectly.

## II

The Examiner also maintained the rejection against claims 37-40, 47-50, 54-57, and 60-63 as being obvious over Zhang in view of Miller and Jarman et al., Mol. Cell. Bio. 11(9): 4679-4689 (“Jarman”). See the Office Action, page 4, lines 14-19. Applicant disagrees and discusses independent claims 33 and 51 first, from which the rejected claims depend.

As discussed in Part I above and in the previous response, Zhang and Miller do not suggest a viral vector containing an enhancer. Jarman teaches a regulatory element of the human  $\alpha$  globin gene. It does not teach or suggest making a viral vector containing a regulatory element, such as an enhancer. In other words, it does not rectify the common deficiencies of Zhang and Miller.

Thus, for the same reasons set forth in Part I above, these three references, alone or combined, would have not suggested an enhancer-containing viral vector of claim 33. Claim 33 is therefore non-obvious over the three references. So is claim 51, which covers a method using the vector of claim 33. Claims 37-40, 47-50, 54-57, and 60-63, all of which depend from claims 33 and 51, are also non-obvious in view of these three references.

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(CON)

CONCLUSION

Applicant submits that grounds for the rejections asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that is non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Please apply any other charges to deposit account 06-1050, referencing the Attorney's Docket No. 08919-016003.

Respectfully submitted,

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